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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2  Apr 08  "Ask CAS" for self-help around the clock
 NEWS  3  Apr 09  BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS  4  Apr 09  ZDB will be removed from STN
 NEWS  5  Apr 19  US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS  6  Apr 22  Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS  7  Apr 22  BIOSIS Gene Names now available in TOXCENTER
 NEWS  8  Apr 22  Federal Research in Progress (FEDRIP) now available
 NEWS  9  Jun 03  New e-mail delivery for search results now available
 NEWS 10  Jun 10  MEDLINE Reload
 NEWS 11  Jun 10  PCTFULL has been reloaded
 NEWS 12  Jul 02  FOREGE no longer contains STANDARDS file segment
 NEWS 13  Jul 22  USAN to be reloaded July 28, 2002;
                  saved answer sets no longer valid
 NEWS 14  Jul 29  Enhanced polymer searching in REGISTRY
 NEWS 15  Jul 30  NETFIRST to be removed from STN
 NEWS 16  Aug 08  CANCERLIT reload
 NEWS 17  Aug 08  PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18  Aug 08  NTIS has been reloaded and enhanced
 NEWS 19  Aug 19  Aquatic Toxicity Information Retrieval (AQUIRE)
                  now available on STN
 NEWS 20  Aug 19  IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21  Aug 19  The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22  Aug 26  Sequence searching in REGISTRY enhanced
 NEWS 23  Sep 03  JAPIO has been reloaded and enhanced
 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 26  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 27  Oct 21  EVENTLINE has been reloaded
 NEWS 28  Oct 24  BEILSTEIN adds new search fields
 NEWS 29  Oct 24  Nutraceuticals International (NUTRACEUT) now available on STN
 NEWS 30  Oct 25  MEDLINE SDI run of October 8, 2002
 NEWS 31  Nov 18  DKILIT has been renamed APOLLIT
 NEWS 32  Nov 25  More calculated properties added to REGISTRY
 NEWS 33  Dec 02  TIBKAT will be removed from STN
 NEWS 34  Dec 04  CSA files on STN
 NEWS 35  Dec 17  PCTFULL now covers WP/PCT Applications from 1978 to date
 NEWS 36  Dec 17  TOXCENTER enhanced with additional content
 NEWS 37  Dec 17  Adis Clinical Trials Insight now available on STN
 NEWS 38  Dec 30  ISMEC no longer available
 NEWS 39  Jan 13  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 40  Jan 21  NUTRACEUT offering one free connect hour in February 2003
 NEWS 41  Jan 21  PHARMAML offering one free connect hour in February 2003
 NEWS 42  Jan 29  Simultaneous left and right truncation added to COMPENDEX,
                  ENERGY, INSPEC
 NEWS 43  Feb 13  CANCERLIT is no longer being updated
 NEWS 44  Feb 24  METADEX enhancements
 NEWS 45  Feb 24  PCTGEN now available on STN
 NEWS 46  Feb 24  TEMA now available on STN
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NEWS 47  Feb 26  NTIS now allows simultaneous left and right truncation
NEWS 48  Feb 26  PCTFULL now contains images
NEWS 49  Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results

NEWS EXPRESS  January 6 CURRENT WINDOWS VERSION IS V6.01a,
              CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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FILE 'HOME' ENTERED AT 16:04:17 ON 04 MAR 2003

=> file uspatfull
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'USPATFULL' ENTERED AT 16:04:30 ON 04 MAR 2003
CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 4 Mar 2003 (20030304/PD)
FILE LAST UPDATED: 4 Mar 2003 (20030304/ED)
HIGHEST GRANTED PATENT NUMBER: US6530088
HIGHEST APPLICATION PUBLICATION NUMBER: US2003041363
CA INDEXING IS CURRENT THROUGH 4 Mar 2003 (20030304/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 4 Mar 2003 (20030304/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Dec 2002
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Dec 2002

>>>  USPAT2 is now available.  USPATFULL contains full text of the      <<<
>>>  original, i.e., the earliest published granted patents or          <<<
>>>  applications.  USPAT2 contains full text of the latest US          <<<
>>>  publications, starting in 2001, for the inventions covered in      <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original      <<<
>>>  published document but also a list of any subsequent               <<<
>>>  publications.  The publication number, patent kind code, and       <<<
>>>  publication date for all the US publications for an invention      <<<
>>>  are displayed in the PI (Patent Information) field of USPATFULL    <<<
>>>  records and may be searched in standard search fields, e.g., /PN,  <<<
>>>  /PK, etc.                                                          <<<

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>>>                                                                     <<<
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>>>  Use USPATALL when searching terms such as patent assignees,        <<<
>>>  classifications, or claims, that may potentially change from       <<<
>>>  the earliest to the latest publication.                            <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s stem cells and nitric oxide
        126332 STEM
        319013 CELLS
          9569 STEM CELLS
                 (STEM(W)CELLS)
         67061 NITRIC
        475839 OXIDE
          6927 NITRIC OXIDE
                 (NITRIC(W)OXIDE)
L1         507 STEM CELLS AND NITRIC OXIDE

=> s l1 and hematopoiesis
          2016 HEMATOPOIESIS
L2         189 L1 AND HEMATOPOIESIS

=> s l2 and nitric oxide synthase
         67061 NITRIC
        475839 OXIDE
          9133 SYNTHASE
          1387 NITRIC OXIDE SYNTHASE
                 (NITRIC(W)OXIDE(W)SYNTHASE)
L3         142 L2 AND NITRIC OXIDE SYNTHASE

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=> s l3 and pd<2000
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L5           2 L3 AND PD<2000

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L2   ANSWER 1 OF 189  USPATFULL
AN     2003:57533  USPATFULL
TI     Serpin polynucleotides, polypeptides, and antibodies
IN     Ruben, Steven M., Olney, MD, UNITED STATES
       Ni, Jian, Germantown, MD, UNITED STATES
PA     Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
       corporation)
PI     US 2003040097      A1   20030227
AI     US 2002-116166     A1   20020405 (10)
RLI    Continuation of Ser. No. US 2000-641721, filed on 21 Aug 2000, PENDING
       Continuation-in-part of Ser. No. WO 2000-US5082, filed on 29 Feb 2000,
       UNKNOWN
PRAI   US 1999-122276P     19990301 (60)
       US 1999-124094P     19990312 (60)
       US 1999-149452P     19990818 (60)
DT     Utility
FS     APPLICATION
LN.CNT 8865
INCL   INCLM: 435/226.000
       INCLS: 435/320.100; 435/325.000; 435/069.100; 536/023.200; 435/184.000
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NCL     NCLM:  435/226.000
        NCLS:  435/320.100; 435/325.000; 435/069.100; 536/023.200; 435/184.000
IC      [7]
        ICM: C12N009-64
        ICS: C12N009-99; C07H021-04; C12P021-02; C12N005-06

L2    ANSWER 2 OF 189  USPATFULL
AN      2003:57524  USPATFULL
TI      Secreted protein HT5GJ57
IN      Ruben, Steven M., Olney, MD, UNITED STATES
        Komatsoulis, George, Silver Spring, MD, UNITED STATES
        Duan, Roxanne D., Bethesda, MD, UNITED STATES
        Rosen, Craig A., Laytonsville, MD, UNITED STATES
        Moore, Paul A., Germantown, MD, UNITED STATES
        Shi, Yanggu, Gaithersburg, MD, UNITED STATES
        LaFleur, David W., Washington, DC, UNITED STATES
        Ebner, Reinhard, Gaithersburg, MD, UNITED STATES
        Olsen, Henrik S., Gaithersburg, MD, UNITED STATES
        Brewer, Laurie A., St. Paul, MN, UNITED STATES
        Florence, Kimberly A., Rockville, MD, UNITED STATES
        Young, Paul E., Gaithersburg, MD, UNITED STATES
        Mucenski, Michael, Cincinnati, OH, UNITED STATES
        Endress, Gregory A., Florence, MA, UNITED STATES
        Soppet, Daniel R., Centreville, VA, UNITED STATES
PA      Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S.
        corporation)
PI      US 2003040088      A1   20030227
AI      US 2001-984271     A1   20011029 (9)
RLI     Division of Ser. No. US 2000-482273, filed on 13 Jan 2000, PENDING
        Continuation-in-part of Ser. No. WO 1999-US15849, filed on 14 Jul 1999,
        UNKNOWN
PRAI    US 1998-92921P      19980715 (60)
        US 1998-92922P      19980715 (60)
        US 1998-92956P      19980715 (60)
DT      Utility
FS      APPLICATION
LN.CNT 24720
INCL    INCLM: 435/183.000
        INCLS: 435/006.000; 435/069.100; 435/325.000; 435/320.100; 530/350.000;
               536/023.200
NCL     NCLM:  435/183.000
        NCLS:  435/006.000; 435/069.100; 435/325.000; 435/320.100; 530/350.000;
               536/023.200
IC      [7]
        ICM: C12Q001-68
        ICS: C07H021-04; C12N009-00; C12P021-02; C12N005-06


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     FILE 'USPATFULL' ENTERED AT 16:04:30 ON 04 MAR 2003
L1          507 S STEM CELLS AND NITRIC OXIDE
L2          189 S L1 AND HEMATOPOIESIS
L3          142 S L2 AND NITRIC OXIDE SYNTHASE
L4            0 S L3 AND PD<1999
L5            2 S L3 AND PD<2000

=> d l5 1-2 bib, kwic

L5    ANSWER 1 OF 2  USPATFULL
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AN   1999:141294 USPATFULL
TI   Methods for enhancing angiogenesis with endothelial progenitor cells
IN   Isner, Jeffrey M., Weston, MA, United States
        Asahara, Takayuki, Arlington, MA, United States
PA   St. Elizabeth's Medical Center of Boston, Boston, MA, United States
        (U.S. corporation)
PI   US 5980887   19991109   <--
AI   US 1996-744882   19961108 (8)
DT   Utility
FS   Granted
EXNAM   Primary Examiner: Chan, Christina Y.; Assistant Examiner: Gambel,
        Phillip
LREP   Conlin, David G., Resnick, David S.Dike, Bronstein, Roberts & Cushman,
        LLP
CLMN   Number of Claims: 11
ECL   Exemplary Claim: 1
DRWN   43 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 1104
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
PI   US 5980887   19991109   <--
DETD   . . . typically begins as a cluster formation, or blood island,
        comprised of EC progenitors (e.g. angioblasts) at the periphery and
        hematopoietic **stem cells** (HSCs) at the center (3).
        In addition to this intimate and predictable spatial association, such
        EC progenitors and HSCs share. . .
DETD   The demonstration that transplants of HSCs derived from peripheral blood
        can provide sustained hematopoietic recovery constitutes inferential
        evidence for circulating **stem cells**. (5). This
        observation is now being exploited clinically as an alternative to bone
        marrow transplantation.
DETD   . . . genes or their encoded gene products to enhance the activity of
        targeted cells, while simultaneously inducing angiogenesis, including,
        for example, **nitric oxide synthase**,
        L-arginine, fibronectin, urokinase, plasminogen activator and heparin.
DETD   ECs uniquely express endothelial constitutive **nitric**
        oxide synthase (ecNOS). Accordingly, MB.sup.CD34+,
        MB.sup.CD34- and AT.sup.CD34+ were investigated for expression of
        ecNOS by RT-PCR (15). ecNOS mRNA was not detectable. . . however,
        ecNOS mRNA was markedly increased (FIG. 5). Functional evidence of ecNOS
        protein in AT.sup.CD34+ was documented by measurement of **nitric**
        oxide in response to the EC-dependent agonist, acetylcholine
        (Ach), and the EC-specific mitogen, vascular endothelial growth factor
        (VEGF) (16) (FIG. 5);. . .
DETD   Cell-cell interaction is considered to play a decisive role in cell
        signaling, differentiation, and proliferation during
        hematopoiesis (19) and angiogenesis (20). To study the impact of
        MB.sup.CD34+ interaction with mature ECs on the differentiation of
        MB.sup.CD34+ into. . .

L5   ANSWER 2 OF 2 USPATFULL
AN   1999:137330 USPATFULL
TI   Therapeutic uses for **nitric oxide** inhibitors
IN   Enikolopov, Grigori N., Cold Spring Harbor, NY, United States
        Peunova, Natalia I., Cold Spring Harbor, NY, United States
        Kuzin, Boris A., Moscow, Russian Federation
        Michurina, Tatiyana, Moscow, Russian Federation
PA   Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States
        (U.S. corporation)
PI   US 5977181   19991102   <--
AI   US 1997-969475   19971113 (8)
PRAI   US 1996-30690P   19961113 (60)
        US 1997-45411P   19970502 (60)

DT Utility
FS Granted
EXNAM Primary Examiner: Criares, Theodore J.
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1655
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
TI Therapeutic uses for **nitric oxide** inhibitors
PI US 5977181 19991102 <--
AB The present invention is based on the discovery that **nitric oxide** (NO) is an important growth regulator in an intact developing organism. In particular, the present invention relates to a method of increasing in a mammal a population of hematopoietic **stem cells** in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, wherein the bone marrow is contacted with an inhibitor of NO, such as an inhibitor of **nitric oxide synthase** (NOS), thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The present invention also relates to a method of increasing a population of cells in S phase in. . .
SUMM The present invention is based on the discovery that **nitric oxide** (NO) is an important growth regulator in an intact developing organism. In particular, the present invention relates to a method of increasing in a mammal a population of hematopoietic **stem cells,** including precursors to myeloid, lymphoid and erythroid cells, in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, wherein the bone marrow is contacted with an inhibitor of NO, such as an inhibitor of **nitric oxide synthase** (NOS), thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The method can be carried out in vivo or ex vivo. In addition, the method can be used. . .
SUMM The present invention also relates to a method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation. In the method, the bone marrow of the mammal is contacted with an inhibitor of NOS, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The method can further comprise contacting the bone marrow with at least one agent which induces differentiation of. . .
SUMM In one embodiment of the method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation, bone marroow which is to be transplanted is obtained, wherein the bone marrow to be transplanted can be. . . is transplanted into the mammal being treated, thereby providing the mammal with bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The method can further comprise treating the mammal with an inhibitor of NOS before or after transplanting the. . .
SUMM . . . increasing a population of dividing cells in a tissue of a mammal comprising contacting the cells with an inhibitor of **nitric oxide**. In one embodiment, the present invention also relates to a method of increasing a population of cells in S phase.

SUMM . . . thereby inhibiting differentiation and inducing proliferation of cells of the tissue, then contacting the selected tissue with a compound (e.g., **nitric oxide**, a growth factor or a combination of both) which inhibits proliferation and induced differentiation. In one embodiment, the method involves. . .

SUMM . . . method, bone marrow is contacted with an inhibitor of NOS, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation; and at least one agent (e.g., a hematopoietic growth factor) selected to induce specific differentiation of the hematopoietic. . .

SUMM Results of the work described herein have shown that a transcellular messenger (**nitric oxide** (NO)) plays a critical role in tissue differentiation and organism development. NO regulates the balance between cell proliferation and cell. . .

SUMM Accordingly, the present invention relates to a method of increasing in a mammal a population of hematopoietic **stem cells**, including precursors to myeloid, lymphoid and erythroid cells, in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, by contacting the bone marrow with an inhibitor of NO, such as an inhibitor of NOS. The present invention includes a method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation, in which the bone marrow of the mammal is contacted with an inhibitor of NOS.

SUMM . . . increasing a population of dividing cells in a tissue of a mammal comprising contacting the cells with an inhibitor of **nitric oxide**. In one embodiment, the present invention can also be used to increase a population of cells (targeted cells) in s. . .

SUMM . . . lymphocytes, neutrophils and platelets). For example, in the embodiment wherein a mammal is treated to increase a population of hematopoietic **stem cells** in the bone marrow of the mammal by contacting the bone marrow of the mammal with an inhibitor of NOS,. . .

SUMM . . . balance between cell proliferation and cell differentiation. Moreover, results shown here demonstrate that NO acts as a crucial regulator of **hematopoiesis** after bone marrow (BM) transplantation. NO regulates the maturation of both the erythroid and myeloid lineages. These data demonstrate that manipulations of NOS activity and NO levels during **hematopoiesis** can be used to alter (enhance or reduce) blood cell production. This is useful for preventive and therapeutic intervention.

SUMM As also described herein, the role of NO in **hematopoiesis** was examined. To demonstrate the presence of NOS in the bone marrow (BM) cells, BM from adult mice was tested. . .

SUMM A mouse model of syngeneic BM transfer was used to evaluate the role of NO in **hematopoiesis**. Mice were irradiated to inhibit **hematopoiesis** in the recipient animal, BM was transplanted from syngeneic animals, and the animals were treated with specific NOS inhibitors. This procedure permits the proliferation, differentiation and survival of only the transplanted cells. To study the changes in **hematopoiesis** introduced by NOS inhibitors, the colonies in the spleen were monitored to test the differentiation of erythroid cells, and the. . . of the recipients were monitored to test the differentiation of cells of the granulocyte-macrophage lineage. The role of NO on **hematopoiesis** was tested by injecting the animals with the specific and structurally unrelated NOS inhibitors L-nitroarginine methyl ester (L-NAME), and 2-ethyl-2-thiopseudourea. . .

SUMM Taken together, the results of these studies indicate that NO modulates **hematopoiesis** after BM transplantation. This confirms the role of No as a major regulatory factor in the organism controlling the balance. . .

SUMM The results of work described herein support the ability of NO to act as a crucial regulator of **hematopoiesis** after bone marrow transplantation (BMT). NO regulates maturation of both erythroid and myeloid cell lineages. By interfering with NO production. . . and 20-fold for the erythroid lineage. The data described herein demonstrates that manipulations of NOS activity and NO levels during **hematopoiesis** can be used for therapeutic purposes to influence self renewal and differentiation of hematopoietic **stem cells**, and to replace damaged or defective cells. Areas of application include enhancement of blood cell and myeloid cell formation following. . .

SUMM . . . chondrocyte differentiation. These results show that manipulation of NO production can regulate growth and differentiation of osteoblasts, chondrocytes, or mesenchymal **stem cells** . This can be used for amplification and further differentiation of cells in the injured tissue, or for cell implants (in. . .

DETD **Nitric Oxide** Regulates Cell Proliferation During Drosophila Development

DETD **Nitric Oxide** Regulates **Hematopoiesis** in Animals Erythroid Differentiation

DETD . . . cGy total body irradiation within 3-4 hours before transplantation. This dosage was tested to be enough for complete suppression of **hematopoiesis** in the irradiated recipient animals. BM cells were flushed from the femurs of syngeneic donors and injected intravenously (10.sup.5 BM. . .

DETD . . . granulocyte colony stimulating factor (G-CSF-R) and erythropoietin (EpoR). The appearance of each of these receptors marks a specific stage in **hematopoiesis**.

DETD **Stem Cells** in the Bone Marrow

DETD . . . the presence of various growth factor receptors which serve as markers of the differentiation stage and indicate the presence of **stem cells** and multipotent precursor cells. The BM preparations were tested for cells expressing receptors to HSF (ligand of c-kit), GM-CSF, G-CSF. . . number of c-kit-positive and IL-3-R-positive cells, suggesting that the population of cells in the BM becomes highly enriched in hematopoietic **stem cells**. At the same time the number of cells expressing receptors for G-CSF, which marks the later stages of differentiation, decreases almost three-fold, while the number of GM-CSF-R-positive cells is slightly decreased. This suggests that inhibition of NOS during **hematopoiesis** selectively enriches the BM in undifferentiated **stem cells** which have already acquired c-kit and IL3 receptors, but have not proceeded to the later stages when the receptor for. . .

DETD The critical question is whether undifferentiated **stem cells** which accumulate in the bone marrow as a result of treatment with NOS inhibitors have the capacity to revert to normal state and resume normal **hematopoiesis** process once the action of NOS inhibitors is suspended. The failure to do so might indicate that the cells become. . . with NOS inhibitors was halted 7-9 days after the BM transfer and checked the BM cells for the presence of **hematopoiesis** markers 1-7 days after termination of injections. Control mice continued to receive the daily injections, The results (Table 4) demonstrate. . . cells were able to resume their differentiation and to proceed to the later stages normally. This indicates that enrichment in **stem cells** after treatment with NOS inhibitors is reversible and can be used to "boost" the number of **stem cells** before inducing them to

proceed further along their differentiation pathways.

DETD **Nitric Oxide** Regulates Brain Development In Vertebrates

DETD It has been recently demonstrated that **nitric oxide** (NO), a multifunctional second messenger, is involved in cell and tissue differentiation and organism development. NO synthase (NOS) controls the. . . as a result, regulates the balance between cell proliferation and differentiation in cultured neuronal cells, in developing Drósophila, and during **hematopoiesis** in mammals (Peunova et al., 1996; Kuzin et al., 1996; Michurina et al., 1997). Here, whether NOS is involved in. . .

CLM What is claimed is:

1. A method of increasing in a mammal a population of hematopoietic **stem cells** in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, comprising contacting the bone marrow with an inhibitor of **nitric oxide synthase**, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation.

3. A method according to claim 2 further comprising implanting the bone marrow having an increased population of hematopoietic **stem cells** into a mammal in need thereof.

7. A method according to claim 1 wherein the inhibitor of **nitric oxide synthase** is selected from the group consisting of L-nitroarginine methyl ester, 2-ethyl-2-thiopseudourea, aminoguanidine hemisulfate and N-monomethyl-L-arginine.

8. A method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation, comprising contacting the bone marrow of the mammal with an inhibitor of **nitric oxide synthase**, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation.

10. A method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation, comprising the steps of: a) obtaining bone marrow which is to be transplanted into the mammal; b) contacting the bone marrow to be transplanted with an inhibitor of **nitric oxide synthase**; c) transplanting the bone marrow of step (b) into the mammal to be treated, thereby providing the mammal with bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation.

11. A method according to claim 10 further comprising: d) treating the mammal with an enhancer of **nitric oxide synthase** after transplanting the bone marrow.

12. A method according to claim 10 further comprising: d) treating the mammal with an inhibitor of **nitric oxide synthase** after transplanting the bone marrow.

. . . method of producing a subpopulation of hematopoietic cells comprising the steps of: a) contacting bone marrow with an inhibitor of **nitric oxide synthase**, thereby producing

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        bone marrow having an increased population of hematopoietic **stem
        cells** which are capable of undergoing normal
        **hematopoiesis** and differentiation; and b) contacting the bone
        marrow with at least one hematopoietic growth factor selected to induce
        specific differentiation.  . .


=> s stem cell? and nitric oxide synthase and hematope?
        126332 STEM
        641162 CELL?
         11080 STEM CELL?
                 (STEM(W)CELL?)
         67061 NITRIC
        475839 OXIDE
          9133 SYNTHASE
          1387 NITRIC OXIDE SYNTHASE
                 (NITRIC(W)OXIDE(W)SYNTHASE)
             4 HEMATOPE?
L6           0 STEM CELL? AND NITRIC OXIDE SYNTHASE AND HEMATOPE?

=> s stem cell? and nitric oxide synthase and hematopo?
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                 (STEM(W)CELL?)
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       2434829 PD<1999
                 (PD<19990000)
L8           3 L7 AND PD<1999

=> d 181-3
'L999-3' IS NOT A VALID FORMAT FOR FILE 'USPATFULL'

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DALL ------- ALL, delimited for post-processing
FP --------- PI, TI, IN, INA, PA, PAA, PAT, PTERM, DCD, AI, RLI,
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              NCLM, NCLS, EXF, REP, REN, ARTU, EXNAM, LREP,
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FPG -------- FP plus PAGE.DRAW
GI --------- PN and page image numbers
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              its structure diagram
IABS ------- ABS, indented with text labels
IALL ------- ALL, indented with text labels
IALLG ------ IALL plus PAGE.DRAW
IBIB ------- BIB, indented with text labels
IBIB.EX ---- IBIB for original and latest publication
IBIBG ------ IBIB plus PAGE.DRAW
IMAX ------- MAX, indented with text labels
IMAX.EX ---- IMAX for original and latest publication
IND -------- INCL, INCLM, INCLS, NCL, NCLM, NCLS, IC, ICM, ICS,
              EXF, ARTU, OS, CC, SX, ST, IT
ISTD ------- STD, indented with text labels
KWIC ------- All hit terms plus 20 words on either side
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              EXF, ARTU OS, CC, SX, ST, IT
MAX.EX ----- MAX for original and latest publication
OCC -------- List of display fields containing hit terms
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STD.EX ----- STD for original and latest publication
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'FORMAT' IS NOT A VALID FORMAT FOR FILE 'USPATFULL'

The following are valid formats:

The default display format is STD.

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IBIB.EX ---- IBIB for original and latest publication
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L8    ANSWER 1 OF 3  USPATFULL
AN       1998:68519  USPATFULL
TI       Systemic gene treatment of connective tissue diseases with IRAP-1
IN       Evans, Christopher H., Pittsburgh, PA, United States
         Robbins, Paul D., Pittsburgh, PA, United States
PA       University of Pittsburgh of the Commonwealth System of Higher Education,
         Pittsburgh, PA, United States (U.S. corporation)
PI       US 5766585              19980616                          <--
AI       US 1996-697180          19960820 (8)
RLI      Continuation of Ser. No. US 1993-167642, filed on 14 Dec 1993, now
         abandoned
DT       Utility
FS       Granted
LN.CNT 1869
INCL     INCLM: 424/093.210
         INCLS: 424/093.100; 424/093.200; 424/529.000; 424/534.000; 435/172.300;
                435/320.100; 514/044.000; 935/023.000; 935/071.000
NCL      NCLM:  424/093.210
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                514/044.000
IC       [6]
         ICM: A01N043-04
         ICS: A01N063-00; C12N005-16; C12N015-07
EXF      435/69.1; 435/70.1; 435/703; 435/172.1; 435/172.3; 435/320.1; 435/325;
         424/93.1; 424/93.2; 424/93.21; 424/529; 424/534; 514/44; 935/22; 935/32;
         935/34; 935/70; 935/71; 935/23
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


=> D L8 2-3

L8    ANSWER 2 OF 3  USPATFULL
AN       97:42862  USPATFULL
TI       Method for producing in vivo delivery of therapeutic agents via
         liposomes
IN       Dzau, Victor J., 12101 Dawn La., Los Altos Hills, CA, United States
         94022
         Kaneda, Yasufumi, Molecular & Cellular Institute, Osaka University, 1-3,
         Yamada-oka, Suita-City, Osaka 565, Japan
PI       US 5631237              19970520                          <--
AI       US 1994-241372          19940510 (8)
RLI      Continuation-in-part of Ser. No. US 1992-995022, filed on 22 Dec 1992,
         now abandoned
DT       Utility
FS       Granted
LN.CNT 2435
INCL     INCLM: 514/044.000
         INCLS: 424/450.000; 424/417.000; 428/402.200; 264/004.100; 264/004.300;
                264/004.600
NCL      NCLM:  514/044.000
         NCLS:  264/004.100; 264/004.300; 264/004.600; 424/417.000; 424/450.000;
                428/402.200
IC       [6]
         ICM: A61K048-00
         ICS: A61K009-127
EXF      514/44; 514/2; 424/93.1; 424/450; 424/283.1; 424/1.21; 424/1.25;
         435/320.1; 435/69.1; 435/5; 435/193
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L8    ANSWER 3 OF 3  USPATFULL
AN       95:58172  USPATFULL
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TI      Treatment of vascular degenerative diseases by modulation of endogenous
        nitric oxide production of activity
IN      Cooke, John P., Palo Alto, CA, United States
        Dzau, Victor J., Los Altos Hills, CA, United States
        Gibbons, Gary H., Palo Alto, CA, United States
PA      The Board of Trustees of the Leland Stanford Junior University,
        Stanford, CA, United States (U.S. corporation)
PI      US 5428070              19950627                                <--
AI      US 1993-76312           19930611 (8)
DT      Utility
FS      Granted
LN.CNT 683
INCL    INCLM: 514/557.000
        INCLS: 514/310.000
NCL     NCLM:  514/557.000
        NCLS:  514/310.000
IC      [6]
        ICM: A01N037-00
        ICS: A61K031-19
EXF     514/310; 514/557
CAS INDEXING IS AVAILABLE FOR THIS PATENT.


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        319013 CELLS
          9569 STEM CELLS
                 (STEM(W)CELLS)
         67061 NITRIC
        475839 OXIDE
          9133 SYNTHASE
          1387 NITRIC OXIDE SYNTHASE
                 (NITRIC(W)OXIDE(W)SYNTHASE)
L9           142 HEMATOPOIESIS AND STEM CELLS AND NITRIC OXIDE SYNTHASE

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                 (PD<19990000)
L10            0 L9 AND PD<1999

=> S L9 AND PD< 2000
       2604557 PD< 2000
                 (PD<20000000)
L11            2 L9 AND PD< 2000

=> D L11 1-2

L11  ANSWER 1 OF 2  USPATFULL
AN      1999:141294  USPATFULL
TI      Methods for enhancing angiogenesis with endothelial progenitor cells
IN      Isner, Jeffrey M., Weston, MA, United States
        Asahara, Takayuki, Arlington, MA, United States
PA      St. Elizabeth's Medical Center of Boston, Boston, MA, United States
        (U.S. corporation)
PI      US 5980887              19991109                                <--
AI      US 1996-744882          19961108 (8)
DT      Utility
FS      Granted
LN.CNT 1104
INCL    INCLM: 424/093.700
        INCLS: 424/085.100; 424/085.200; 514/008.000; 514/044.000
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NCL   NCLM: 424/093.700
        NCLS: 424/085.100; 424/085.200; 514/008.000; 514/044.000
IC   [6]
        ICM: A61K035-12
        ICS: A61K048-00; A61K038-18; A61K038-19
EXF   424/93.7; 424/85.4; 424/85.2; 435/325; 435/375; 514/2; 514/8; 514/44;
        530/351; 053/23.5
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 2 OF 2 USPATFULL
AN   1999:137330 USPATFULL
TI   Therapeutic uses for nitric oxide inhibitors
IN   Enikolopov, Grigori N., Cold Spring Harbor, NY, United States
        Peunova, Natalia I., Cold Spring Harbor, NY, United States
        Kuzin, Boris A., Moscow, Russian Federation
        Michurina, Tatiyana, Moscow, Russian Federation
PA   Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, United States
        (U.S. corporation)
PI   US 5977181   19991102   <--
AI   US 1997-969475   19971113 (8)
PRAI   US 1996-30690P   19961113 (60)
        US 1997-45411P   19970502 (60)
DT   Utility
FS   Granted
LN.CNT 1655
INCL   INCLM: 514/631.000
        INCLS: 514/565.000; 514/632.000
NCL   NCLM: 514/631.000
        NCLS: 514/565.000; 514/632.000
IC   [6]
        ICM: A61K031-195
        ICS: A61K031-155
EXF   514/565; 514/631; 514/632
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> D L11 1-2 KWIC

L11 ANSWER 1 OF 2 USPATFULL
PI   US 5980887   19991109   <--
DETD   . . . . typically begins as a cluster formation, or blood island,
        comprised of EC progenitors (e.g. angioblasts) at the periphery and
        hematopoietic **stem cells** (HSCs) at the center (3).
        In addition to this intimate and predictable spatial association, such
        EC progenitors and HSCs share. . .
DETD   The demonstration that transplants of HSCs derived from peripheral blood
        can provide sustained hematopoietic recovery constitutes inferential
        evidence for circulating **stem cells**. (5). This
        observation is now being exploited clinically as an alternative to bone
        marrow transplantation.
DETD   . . . . genes or their encoded gene products to enhance the activity of
        targeted cells, while simultaneously inducing angiogenesis, including,
        for example, **nitric oxide synthase**,
        L-arginine, fibronectin, urokinase, plasminogen activator and heparin.
DETD   ECs uniquely express endothelial constitutive **nitric
        oxide synthase** (ecNOS). Accordingly, MB.sup.CD34+,
        MB.sup.CD34- and AT.sup.CD34+ were investigated for expression of
        ecNOS by RT-PCR (15). ecNOS mRNA was not detectable. . .
DETD   Cell-cell interaction is considered to play a decisive role in cell
        signaling, differentiation, and proliferation during
        hematopoiesis (19) and angiogenesis (20). To study the impact of
        MB.sup.CD34+ interaction with mature ECs on the differentiation of

MB.sup.CD34+ into. . .

L11 ANSWER 2 OF 2 USPATFULL
PI US 5977181 19991102 <--
AB . . . developing organism. In particular, the present invention relates to a method of increasing in a mammal a population of hematopoietic **stem cells** in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, wherein the bone marrow is contacted with an inhibitor of NO, such as an inhibitor of **nitric oxide synthase** (NOS), thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The present invention also relates to a method of increasing a population of cells in S phase in. . .

SUMM . . . developing organism. In particular, the present invention relates to a method of increasing in a mammal a population of hematopoietic **stem cells**, including precursors to myeloid, lymphoid and erythroid cells, in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, wherein the bone marrow is contacted with an inhibitor of NO, such as an inhibitor of **nitric oxide synthase** (NOS), thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The method can be carried out in vivo or ex vivo. In addition, the method can be used. . .

SUMM The present invention also relates to a method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation. In the method, the bone marrow of the mammal is contacted with an inhibitor of NOS, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The method can further comprise contacting the bone marrow with at least one agent which induces differentiation of. . .

SUMM In one embodiment of the method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation, bone marroow which is to be transplanted is obtained, wherein the bone marrow to be transplanted can be. . . is transplanted into the mammal being treated, thereby providing the mammal with bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation. The method can further comprise treating the mammal with an inhibitor of NOS before or after transplanting the. . .

SUMM . . . method, bone marrow is contacted with an inhibitor of NOS, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation; and at least one agent (e.g., a hematopoietic growth factor) selected to induce specific differentiation of the hematopoietic. . .

SUMM Accordingly, the present invention relates to a method of increasing in a mammal a population of hematopoietic **stem cells**, including precursors to myeloid, lymphoid and erythroid cells, in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, by contacting the bone marrow with an inhibitor of NO, such as an inhibitor of NOS. The present invention includes a method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are

capable of undergoing normal **hematopoiesis** and differentiation, in which the bone marrow of the mammal is contacted with an inhibitor of NOS.

SUMM . . . lymphocytes, neutrophils and platelets). For example, in the embodiment wherein a mammal is treated to increase a population of hematopoietic **stem cells** in the bone marrow of the mammal by contacting the bone marrow of the mammal with an inhibitor of NOS,. . .

SUMM . . . balance between cell proliferation and cell differentiation. Moreover, results shown here demonstrate that NO acts as a crucial regulator of **hematopoiesis** after bone marrow (BM) transplantation. NO regulates the maturation of both the erythroid and myeloid lineages. These data demonstrate that manipulations of NOS activity and NO levels during **hematopoiesis** can be used to alter (enhance or reduce) blood cell production. This is useful for preventive and therapeutic intervention.

SUMM As also described herein, the role of NO in **hematopoiesis** was examined. To demonstrate the presence of NOS in the bone marrow (BM) cells, BM from adult mice was tested. . .

SUMM A mouse model of syngeneic BM transfer was used to evaluate the role of NO in **hematopoiesis**. Mice were irradiated to inhibit **hematopoiesis** in the recipient animal, BM was transplanted from syngeneic animals, and the animals were treated with specific NOS inhibitors. This procedure permits the proliferation, differentiation and survival of only the transplanted cells. To study the changes in **hematopoiesis** introduced by NOS inhibitors, the colonies in the spleen were monitored to test the differentiation of erythroid cells, and the. . . of the recipients were monitored to test the differentiation of cells of the granulocyte-macrophage lineage. The role of NO on **hematopoiesis** was tested by injecting the animals with the specific and structurally unrelated NOS inhibitors L-nitroarginine methyl ester (L-NAME), and 2-ethyl-2-thiopseudourea. . .

SUMM Taken together, the results of these studies indicate that NO modulates **hematopoiesis** after BM transplantation. This confirms the role of No as a major regulatory factor in the organism controlling the balance. . .

SUMM The results of work described herein support the ability of NO to act as a crucial regulator of **hematopoiesis** after bone marrow transplantation (BMT). NO regulates maturation of both erythroid and myeloid cell lineages. By interfering with NO production. . . and 20-fold for the erythroid lineage. The data described herein demonstrates that manipulations of NOS activity and NO levels during **hematopoiesis** can be used for therapeutic purposes to influence self renewal and differentiation of hematopoietic **stem cells,** and to replace damaged or defective cells. Areas of application include enhancement of blood cell and myeloid cell formation following. . .

SUMM . . . chondrocyte differentiation. These results show that manipulation of NO production can regulate growth and differentiation of osteoblasts, chondrocytes, or mesenchymal **stem cells**. This can be used for amplification and further differentiation of cells in the injured tissue, or for cell implants (in. . .

DETD Nitric Oxide Regulates **Hematopoiesis** in Animals Erythroid Differentiation

DETD . . . cGy total body irradiation within 3-4 hours before transplantation. This dosage was tested to be enough for complete suppression of **hematopoiesis** in the irradiated recipient animals. BM cells were flushed from the femurs of syngeneic donors and injected intravenously (10.sup.5 BM. . .

DETD . . . granulocyte colony stimulating factor (G-CSF-R) and erythropoietin (EpoR). The appearance of each of these receptors marks a

specific stage in **hematopoiesis**.

DETD **Stem Cells** in the Bone Marrow

DETD . . . the presence of various growth factor receptors which serve as markers of the differentiation stage and indicate the presence of **stem cells** and multipotent precursor cells. The BM preparations were tested for cells expressing receptors to HSF (ligand of c-kit), GM-CSF, G-CSF. . . . number of c-kit-positive and IL-3-R-positive cells, suggesting that the population of cells in the BM becomes highly enriched in hematopoietic **stem cells**. At the same time the number of cells expressing receptors for G-CSF, which marks the later stages of differentiation, decreases almost three-fold, while the number of GM-CSF-R-positive cells is slightly decreased. This suggests that inhibition of NOS during **hematopoiesis** selectively enriches the BM in undifferentiated **stem cells** which have already acquired c-kit and IL3 receptors, but have not proceeded to the later stages when the receptor for. . .

DETD The critical question is whether undifferentiated **stem cells** which accumulate in the bone marrow as a result of treatment with NOS inhibitors have the capacity to revert to normal state and resume normal **hematopoiesis** process once the action of NOS inhibitors is suspended. The failure to do so might indicate that the cells become. . . . with NOS inhibitors was halted 7-9 days after the BM transfer and checked the BM cells for the presence of **hematopoiesis** markers 1-7 days after termination of injections. Control mice continued to receive the daily injections, The results (Table 4) demonstrate. . . . cells were able to resume their differentiation and to proceed to the later stages normally. This indicates that enrichment in **stem cells** after treatment with NOS inhibitors is reversible and can be used to "boost" the number of **stem cells** before inducing them to proceed further along their differentiation pathways.

DETD . . . as a result, regulates the balance between cell proliferation and differentiation in cultured neuronal cells, in developing Drosophila, and during **hematopoiesis** in mammals (Peunova et al., 1996; Kuzin et al., 1996; Michurina et al., 1997). Here, whether NOS is involved in. . .

CLM What is claimed is:

1. A method of increasing in a mammal a population of hematopoietic **stem cells** in bone marrow which are capable of undergoing normal **hematopoiesis** and differentiation, comprising contacting the bone marrow with an inhibitor of **nitric oxide synthase**, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation.

3. A method according to claim 2 further comprising implanting the bone marrow having an increased population of hematopoietic **stem cells** into a mammal in need thereof.

7. A method according to claim 1 wherein the inhibitor of **nitric oxide synthase** is selected from the group consisting of L-nitroarginine methyl ester, 2-ethyl-2-thiopseudourea, aminoguanidine hemisulfate and N-monomethyl-L-arginine.

8. A method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation, comprising contacting the bone marrow of the mammal with an inhibitor of **nitric oxide synthase**, thereby producing bone marrow having an increased population of

hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation.

10. A method for treating a mammal to increase a population of hematopoietic **stem cells** in bone marrow of the mammal which are capable of undergoing normal **hematopoiesis** and differentiation, comprising the steps of: a) obtaining bone marrow which is to be transplanted into the mammal; b) contacting the bone marrow to be transplanted with an inhibitor of **nitric oxide synthase**; c) transplanting the bone marrow of step (b) into the mammal to be treated, thereby providing the mammal with bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation.

11. A method according to claim 10 further comprising: d) treating the mammal with an enhancer of **nitric oxide synthase** after transplanting the bone marrow.

12. A method according to claim 10 further comprising: d) treating the mammal with an inhibitor of **nitric oxide synthase** after transplanting the bone marrow.

. . . . method of producing a subpopulation of hematopoietic cells comprising the steps of: a) contacting bone marrow with an inhibitor of **nitric oxide synthase**, thereby producing bone marrow having an increased population of hematopoietic **stem cells** which are capable of undergoing normal **hematopoiesis** and differentiation; and b) contacting the bone marrow with at least one hematopoietic growth factor selected to induce specific differentiation. . . .